# WAS gene

Wiskott-Aldrich syndrome

## Normal Function

The *WAS* gene provides instructions for making a protein called WASP. This protein is found in all blood cells. WASP is involved in relaying signals from the surface of blood cells to the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. WASP signaling activates the cell when it is needed and triggers its movement (motility) and attachment to other cells and tissues (adhesion). In white blood cells, which protect the body from infection, this signaling allows the actin cytoskeleton to establish the interaction between cells and the foreign invaders that they target (immune synapse).

## Health Conditions Related to Genetic Changes

severe congenital neutropenia

Wiskott-Aldrich syndrome

More than 350 mutations in the *WAS* gene have been found to cause Wiskott-Aldrich syndrome, a condition characterized by a reduced ability to form blood clots and abnormal immune system function (immune deficiency). Most of these mutations lead to the production of an abnormally short, nonfunctional version of WASP or prevent the production of any WASP. As a result, WASP cannot relay signals, which disrupts the function of the actin cytoskeleton in developing blood cells. White blood cells that lack WASP have a decreased ability to respond to their environment and form immune synapses. As a result, white blood cells are less able to respond to foreign invaders, causing many of the immune problems related to Wiskott-Aldrich syndrome. Similarly, when cells that aid blood clot formation (platelets) lack functional WASP, their development is impaired, leading to a reduction in platelet size and early cell death. The impairments of white blood cells and platelets are largely responsible for the immune deficiency and bleeding problems characteristic of Wiskott-Aldrich syndrome.

X-linked thrombocytopenia

More than 60 mutations in the *WAS* gene have been found to cause X-linked thrombocytopenia, a blood disorder characterized by a decrease in the amount and size of platelets, leading to prolonged bleeding episodes. Immune problems such as an increased susceptibility to infections may also occur. Most of these *WAS* gene mutations change single protein building blocks (amino acids) in WASP. Mutations

typically lead to the production of an altered protein that cannot efficiently relay signals from the cell membrane to the actin cytoskeleton. In people with X-linked thrombocytopenia, these signaling problems primarily affect the development of platelets. In some cases, white blood cells are affected. When WASP function is impaired in white blood cells, these cells are less able to respond to foreign invaders and immune disorders are more likely to occur.

Some *WAS* gene mutations cause X-linked thrombocytopenia in some individuals and a related condition called Wiskott-Aldrich syndrome (described above) in others. These mutations usually prevent the production of any WASP. It is unknown why some people with these mutations have the relatively mild features of X-linked thrombocytopenia and others have the severe symptoms of Wiskott-Aldrich syndrome.

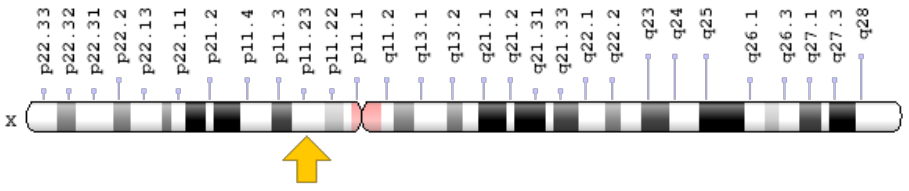
other disorders

Mutations in the *WAS* gene can cause a condition called severe congenital neutropenia, which is characterized by low levels of white blood cells (neutropenia) and decreased survival of hematopoietic stem cells. People with this condition tend to have immune deficiency resulting in recurrent infections. *WAS* gene mutations that cause severe congenital neutropenia lead to a change in a region of WASP known as the Cdc42 binding site. This site must attach (bind) to a protein called Cdc42 in order to turn on (activate) WASP. The mutations that cause severe congenital neutropenia lead to a WASP that is always active (constitutively active), even in the absence of the Cdc42 protein. It is not fully understood how a constitutively active WASP leads to the signs and symptoms of severe congenital neutropenia.

## Chromosomal Location

Cytogenetic Location: Xp11.23, which is the short (p) arm of the X chromosome at position 11.23

Molecular Location: base pairs 48,683,753 to 48,691,427 on the X chromosome (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)




Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- IMD2
- WASP
- WASP_HUMAN
- Wiskott-Aldrich syndrome (eczema-thrombocytopenia)
- Wiskott-Aldrich syndrome protein

## Additional Information & Resources

Educational Resources

- Immunobiology (fifth edition, 2001): Defective T-cell signaling, cytokine production, or cytokine action can cause immunodeficiency.
  https://www.ncbi.nlm.nih.gov/books/NBK27109/#A1510

GeneReviews

- WAS-Related Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK1178

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28WAS%5BTIAB%5D%29+OR+%28WASP%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- NEUTROPENIA, SEVERE CONGENITAL, X-LINKED
  http://omim.org/entry/300299
- WAS GENE
  http://omim.org/entry/300392

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/WASID42801chXp11.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=WAS%5Bgene%5D
- HGNC Gene Family: Wiskott-Aldrich Syndrome protein family
  http://www.genenames.org/cgi-bin/genefamilies/set/14

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12731
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7454
- UniProt
  http://www.uniprot.org/uniprot/P42768

## Sources for This Summary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